

Amendments to the Claims

This listing of claims will replace all prior versions and listings of claims in this application:

Listing of Claims:

Claims 1-6 (Canceled)

7. (Previously presented) The monoclonal antibody of claim 33, wherein the antibody is a scFv.

8. (Previously presented) The monoclonal antibody of claim 33, wherein the antibody is a Fab.

9. (Previously presented) The monoclonal antibody of claim 33, wherein the antibody is a fully assembled antibody.

Claims 10-12 (Canceled)

13. (Withdrawn) A monoclonal antibody that specifically binds to a human VEGF and has V_L comprising the amino acid sequence of

X₁X₂X₃X₄TQX₅PSX₆X₇SX₈X₉X₁₀GX₁₁X₁₂X₁₃X₁₄IX₁₅CX₁₆X₁₇SX₁₈X₁₉IX₂₀X₂₁X₂₂X₂₃X₂₄WYQQX₂₅PGX₂₆APX₂₇X₂₈LX₂₉YX₃₀X₃₁X₃₂X₃₃LX₃₄X₃₅GVX₃₆X₃₇RFSGX₃₈X₃₉SGTDFX₄₀LTIX₄₁X₄₂LQX₄₃X₄₄DX₄₅AX₄₆YYCQQX₄₇X₄₈X₄₉X₅₀PX₅₁TFGX₅₂GTKX₅₃X₅₄IK,
wherein the underlined regions are designated as V_L/CDR1, V_L/CDR2, and V_L/CDR3, respectively, whereas the rest of the region is designated as framework, and wherein X₁ is D, E or A; X₂ is I, or T; X₃ is V, E, K, R, Q, or T; X₄ is M, or L; X₅ is S, or T; X₆ is S, or T; X₇ is L, or V; X₈ is A, or V; X₉ is S, or T; X₁₀ is P, V, L, A, or I; X₁₁ is E, or D; X₁₂ is R, or T; X₁₃ is A, or V I; X₁₄ is T, or A; X₁₅ is T, S, or A; X₁₆ is S, R, N, K, H, or Q; X₁₇ is A, or S; X₁₈ is Q, or R; X₁₉ is S, D, A, or P; X₂₀ is S, G, R, T, or Y; X₂₁ is T, N, S, D, or K; X₂₂ is Y, or D; X₂₃ is L, or I; X₂₄ is A, N, or T; X₂₅ is K, or I; X₂₆ is Q, K, T, or I; X₂₇ is R, K, Q, N, H, S, or E; X₂₈ is V, or L; X₂₉ is I, or V; X₃₀ is F, A, G, D, or S; X₃₁ is A, or T; X₃₂ is S, or T; X₃₃ is N, S, R, or T; X₃₄ is A, H, or Q; X₃₅ is S, or G; X₃₆ is P, T; X₃₇ is S, N, D, G, or Y; X₃₈ is S, or T; X₃₉ is G, or R; X₄₀ is T, or A; X₄₁ is S, or R; X₄₂ is S, or R; X₄₃ is P, or A; X₄₄

is E , or D; X₄₅ is F, V, or S; X₄₆ is V, T, I, A, or S; X₄₇ is Y, or S; X₄₈ is S, Y, or N; X₄₉ is S, or T; X₅₀ is T, V, A, P, K, G, S, or I; X₅₁ is W, or Y; X₅₂ is Q, or G; X₅₃ is V, or L; and X₅₄ is E, D, or A.

14. (Withdrawn) A monoclonal antibody that specifically binds to a human VEGF and has V_L comprising the amino acid sequence of

X₁X₂X₃LTQPPSX₄SX₅TPGQX₆VTISCSGX₇X₈SNX₉GX₁₀NX₁₁VX₁₂WYQQX₁₃P
GX₁₄APKX₁₅LX₁₆YX₁₇NX₁₈X₁₉RPSGVPX₂₀RX₂₁SGSX₂₂SX₂₃TSASLAISGLX₂₄SEDEADY
YCX₂₅X₂₆WDDSLX₂₇GYVFGX₂₈GTX₂₉LTVL, wherein the underlined regions are
designated as V_L/CDR1, V_L/CDR2, and V_L/CDR3, respectively, whereas the rest of the
region is designated as framework, and wherein X₁ is Q, L, or N; X₂ is P, A, F, or S; X₃ is V, or
M; X₄ is A, or T; X₅ is G, or A; X₆ is R, or S; X₇ is S, or T; X₈ is S, T, Y, or N; X₉ is I, or V;
X₁₀ is S, or R; X₁₁ is S, P, N, A, or T; X₁₂ is N, T, or Y; X₁₃ is L, or F; X₁₄ is T, or A; X₁₅ is
V, L, or F; X₁₆ is M, or I; X₁₇ is G, T, or S; X₁₈ is N, or D; X₁₉ is Q, or E; X₂₀ is D, or E; X₂₁
is F, or L; X₂₂ is K, or R; X₂₃ is G, or A; X₂₄ is Q, L, or R; X₂₅ is A, or G; X₂₆ is A, S, or T;
X₂₇ is N, S, or T; X₂₈ is T, or A; and X₂₉ is K, or Q.

15. (Withdrawn) A monoclonal antibody that specifically binds to a human VEGF and has V_L comprising the amino acid sequence of

QSALTQPPSVSGAPGQRVTISCTGRSSNIGAGHDVHWYQQLPGTAPKLLIY
ANDQRPSGVPDRFSDSKSGTSASLGISGLRSEDEADYFCATWDDSLHGYVFGTGTKV
TVL (SEQ ID No: 54).

16. (Withdrawn) A monoclonal antibody is provided that specifically binds to a human VEGF and has V_H comprising the amino acid sequence of

X₁X₂QLVX₃SGGGX₄VQPGGX₅LRLX₆CAX₇SGX₈X₉X₁₀X₁₁X₁₂X₁₃GX₁₄NWX₁₅
RQAPGKGX₁₆EWVGWX₁₇NTX₁₈X₁₉GX₂₀X₂₁TYX₂₂X₂₃X₂₄FX₂₅RRX₂₆TX₂₇SX₂₈X₂₉X₃₀SK
X₃₁X₃₂X₃₃YLQX₃₄NSLRAEDTAVYYCAX₃₅YPX₃₆YYGX₃₇SHWYFDVWX₃₈QGTLVTVS
S, wherein the underlined regions are designated as CDR1, CDR2, and CDR3, respectively,
whereas the rest of the region is designated as framework according to Kabat nomenclature,
and wherein X₁ is E, or Q; X₂ is V, or G; X₃ is Q, or E; X₄ is V, or L; X₅ is S, or T; X₆ is S, T,
or R; X₇ is A, or V; X₈ is Y, or F; X₉ is T, D, N, S, or A; X₁₀ is F, or L; X₁₁ is T, D, Y, A, S,
or N; X₁₂ is N, H, or S; X₁₃ is Y, or F; X₁₄ is M, L, I, or V; X₁₅ is I, V, or L; X₁₆ is L, or P;

X₁₇ is I, or V; X₁₈ is Y, or N; X₁₉ is T, or N; X₂₀ is E, or A; X₂₁ is P, T, or S; X₂₂ is A, or V; X₂₃ is A, H, Q, P, D, or E; X₂₄ is D, or E; X₂₅ is K, or T; X₂₆ is V, F, or L; X₂₇ is F, or I; X₂₈ is L, or R; X₂₉ is D, or N; X₃₀ is T, or N; X₃₁ is S, or N; X₃₂ is T, Q, P, or K; X₃₃ is A, V, or P; X₃₄ is L, or M; X₃₅ is K, or R; X₃₆ is H, or Y; X₃₇ is S, R, or T; and X₃₈ is G, or A.

17. (Withdrawn) A monoclonal antibody is provided that specifically binds to a human VEGF and has V_L comprising the amino acid sequence selected from the group consisting of SEQ ID NOs:2-54, more preferably comprising the amino acid sequence selected from the group consisting of SEQ ID NO:14, SEQ ID NO:26, SEQ ID NO:28, SEQ ID NO:36, SEQ ID NO:37, SEQ ID NO:44, SEQ ID NO:47, and SEQ ID NO:54.

18. (Withdrawn) A monoclonal antibody that specifically binds to a human VEGF and has V_H comprising the amino acid sequence selected from the group consisting of SEQ ID NOs:57-110 and SEQ ID NOs:285-310, and preferably comprising the amino acid sequence selected from the group consisting of SEQ ID NOs:61-64, SEQ ID NO:67, 68, 70, 75, 83, 88, 89, 90, 91, 92, 93, 94, and 96-110.

19. (Withdrawn) A monoclonal antibody is provided that specifically binds to a human VEGF and has CDR2 in the V_L region (V_L/CDR2) comprising the amino acid sequence selected from the group consisting of SEQ ID NOs:195-209.

20. (Withdrawn) A monoclonal antibody that specifically binds to a human VEGF and has CDR3 in the V_L region (V_L/CDR3) comprising the amino acid sequence selected from the group consisting of SEQ ID NOs:210-228.

21. (Withdrawn) A monoclonal antibody that specifically binds to a human VEGF and has a framework region (FR) CDR3 in the V_L region (V_L/FR) comprising the amino acid sequence selected from the group consisting of: SEQ ID NO:229-269, and preferably comprising the amino acid sequence selected from the group consisting of SEQ ID NO:232, 235, 237, 251, 255, 263, and 265.

22. (Withdrawn) A monoclonal antibody that specifically binds to a human VEGF and has CDR1 in the V_H region (V_H/CDR1) comprising the amino acid sequence of

GX₁X₂X₃X₄X₅X₆GX₇N, wherein X₁ is Y, or F; X₂ is D, N, T, S, or A; X₃ is F, or L; X₄ is T, D, S, Y, A, or N; X₅ is H, N, or S; X₆ is Y, or F; X₇ is M, L, I, or V.

23. (Withdrawn) A monoclonal antibody that specifically binds to a human VEGF and has CDR2 in the V_H region (V_H/CDR2) comprising the amino acid sequence of WX₁NTX₂X₃GEX₄TYX₅X₆X₇FX₈R, wherein X₁ is I, or V; X₂ is Y, or N; X₃ is T, or N; X₄ is P, T, or S; X₅ is A, or V; X₆ is A, Q, P, H, D, or E; X₇ is D, or E; and X₈ is K, or T.

24. (Withdrawn) A monoclonal antibody that specifically binds to a human VEGF and has CDR2 in the V_H region (V_H/CDR2) comprising the amino acid sequence selected from the group consisting of: SEQ ID NOs:136-156.

25. (Withdrawn) A monoclonal antibody that specifically binds to a human VEGF and has CDR3 in the V_H region (V_H/CDR3) comprising the amino acid sequence of KYPX₁YYGX₂SHWYFDV, wherein X₁ is Y, or H, and X₂ is R.

26. (Withdrawn) A monoclonal antibody that specifically binds to a human VEGF and has CDR3 in the V_H region (V_H/CDR3) comprising the amino acid sequence selected from the group consisting of SEQ ID NOs:311-337.

27. (Withdrawn) A monoclonal antibody that specifically binds to a human VEGF and has FR in the V_H region (V_H/FR) comprising the amino acid sequence of X₁VQLVX₂SGGGX₃VQPGGX₄LRLX₅CAX₆S/CDR1/WX₇RQAPGKGGLEWVG/CDR2/RX₈TX₉SX₁₀DX₁₁SKX₁₂X₁₃X₁₄YLQX₁₅NSLRAEDTAVYYCA/CDR3/WX₁₆QGTLVTVSS, wherein X₁ is E, or Q; X₂ is Q, or E; X₃ is V, or L; X₄ is S, or T; X₅ is S, T, or R; X₆ is A, or V; X₇ is I, or V; X₈ is F, or V; X₉ is F, or I; X₁₀ is L, or R; X₁₁ is T, or N; X₁₂ is S, or N; X₁₃ is T, Q, or K; X₁₄ is A, or V; X₁₅ is M, or L; and X₁₆ is G, or A.

28. (Previously Presented) A monoclonal antibody that specifically binds to a human VEGF and has a V_L and V_H pair selected from the group consisting of: SEQ ID NO:28 and 88; SEQ ID NO:28 and 90; SEQ ID NO:28 and 91; SEQ ID NO:28 and 106; SEQ ID NO:28 and 107; SEQ ID NO:28 and 108; and SEQ ID NO:28 and 109.

29. (Withdrawn) The monoclonal antibody of any of claims 14-29, wherein the antibody has dissociation constant K_d equal to or lower than 10 nM.

30. (Withdrawn) The monoclonal antibody of any of claims 14-29, wherein the antibody has dissociation constant K_d equal to or lower than 1 nM.

31. (Withdrawn) The monoclonal antibody of any of claims 14-29, wherein the antibody has dissociation constant K_d equal to or lower than 0.1 nM.

32. (Withdrawn) The monoclonal antibody of any of claims 14-29, wherein the antibody has dissociation constant K_d equal to or lower than 0.01 nM.

33. (Previously presented) A monoclonal antibody that specifically binds to human VEGF and has a VL and VH pair selected from the group consisting of: SEQ ID NO:26 and 88; SEQ ID NO:26 and 90; SEQ ID NO:26 and 91; SEQ ID NO:26 and 106; SEQ ID NO:26 and 107; SEQ ID NO:26 and 108; SEQ ID NO:26 and 109; SEQ ID NO:28 and 88; SEQ ID NO:28 and 90; SEQ ID NO:28 and 91; SEQ ID NO:28 and 106; SEQ ID NO:28 and 107; SEQ ID NO:28 and 108; SEQ ID NO:28 and 109; SEQ ID NO:36 and 88; SEQ ID NO:36 and 90; SEQ ID NO:36 and 91; SEQ ID NO:36 and 106; SEQ ID NO:36 and 107; SEQ ID NO:36 and 108; and SEQ ID NO:36 and 109.

34. (Previously presented) A monoclonal antibody that specifically binds to human VEGF and has a VL and VH pair selected from the group consisting of: SEQ ID NO:26 and 106; SEQ ID NO:28 and 106; and SEQ ID NO:36 and 106.

35. (Previously presented) A monoclonal antibody that specifically binds to human VEGF and has a V_L and V_H pair consisting of SEQ ID NO:28 and 106.

36. (Previously presented) A monoclonal antibody that specifically binds to human VEGF and has a VL domain consisting of SEQ ID NO:28 in combination with a VH domain selected from SEQ ID NO: 106, SEQ ID NO: 107, SEQ ID NO:108, SEQ ID NO: 109, SEQ ID NO: 88, SEQ ID NO: 90, and SEQ ID NO: 91 .

37. (Previously presented) The monoclonal antibody of claim 35, wherein the antibody is a scFv.

38. (Previously presented) The monoclonal antibody of claim 35, wherein the antibody is a Fab.

39. (Previously presented) The monoclonal antibody of claim 35, wherein the antibody is a fully assembled antibody.

40. (Currently amended) A ~~monoclonal~~ recombinant antibody that specifically binds to [[a]] human VEGF and has a light chain variable domain (V_L) comprising CDR1, CDR2 and CDR3 regions consisting of the amino acid sequences set forth in SEQ ID NO: 172, SEQ ID NO: 195 and SEQ ID NO: 212, respectively.

41. (Currently amended) The ~~monoclonal~~ recombinant antibody according to claim 40, wherein the heavy chain variable domain (V_H) comprises CDR1, CDR2, and CDR3 regions consisting of the amino acid sequences set forth in SEQ ID NO: 31, SEQ ID NO: 152 and SEQ ID NO: 327, respectively.

42. (Currently amended) The ~~monoclonal~~ recombinant antibody of claim 41, wherein the antibody is a scFv.

43. (Currently amended) The ~~monoclonal~~ recombinant antibody of claim 41, wherein the antibody is a Fab.

44. (Currently amended) The ~~monoclonal~~ recombinant antibody of claim 41, wherein the antibody is a fully assembled antibody.

45. (Currently amended) A ~~monoclonal~~ recombinant antibody that specifically binds to [[a]] human VEGF and has a V_L domain comprising CDR1, CDR2 and CDR3 regions consisting of the amino acid sequences set forth in SEQ ID NO: 170, SEQ ID NO: 195 and SEQ ID NO: 214, respectively.

46. (Currently amended) A ~~monoclonal~~ recombinant antibody that specifically binds to [[a]] human VEGF and has a ~~heavy chain variable~~ V_H domain ~~which comprises~~ comprising CDR1, CDR2, and CDR3 regions consisting of the amino acid sequences set forth in SEQ ID NO: 31, SEQ ID NO: 152 and SEQ ID NO: 327, respectively.

47. (Currently amended) A ~~monoclonal~~ recombinant antibody that specifically binds to [[a]] human VEGF and has V_L comprising CDR1, CDR2 and CDR3 regions consisting of the amino acid sequences set forth in SEQ ID NO: 182, SEQ ID NO: 201 and SEQ ID NO: 222, respectively.

48. (Previously presented) An antibody heavy chain variable domain (VH) consisting of an amino acid sequence selected from SEQ ID NO: 88, SEQ ID NO: 90, SEQ ID NO: 91, SEQ ID NO: 106, SEQ ID NO: 107, SEQ ID NO: 108 and SEQ ID NO: 109.

49. (Previously presented) An antibody light chain variable domain (VL) consisting of an amino acid sequence selected from SEQ ID NO: 26, SEQ ID NO: 28, and SEQ ID NO: 36.